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Original article

Comparison of nutritional screening parameters in oncology patients with malnutrition: handgrip strength as a reliable parameter

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Summary. *Aim:* To evaluate handgrip strength (HGS), phase angle (PA), serum albumin, nutritional risk screening (NRS) and quality of life (QoL) as markers for nutritional status and prognostic factors for survival in oncology patients with malnutrition and parenteral nutritional therapy. *Methods:* We conducted a prospective study with 36 patients between August 2013 and November 2015. HGS was measured using a hydraulic dynamometer, PA was calculated based on bioelectrical impedance tests. Serum albumin levels were measured and a nutritional risk screening (NRS 2002) was performed. The Short Form 12 (SF-12) questionnaire was used to assess QoL. PA was regarded as the gold standard for determining body composition and nutritional status. A 1-year follow-up was performed, and patient survival was evaluated. *Results:* HGS showed a significant correlation with PA in bioelectrical impedance analysis. Body mass index (BMI) was not correlated with HGS. Albumin and NRS showed poor specificity as compared to PA. QoL was not correlated with parameters for nutritional status. Overall survival was poor with a 1-year survival rate of 15%. *Conclusions:* Compared to serum albumin and BMI, HGS is a reliable tool for the assessment of nutritional status in oncology patients. When indication for parenteral nutrition is confirmed in cancer patients with malnutrition, overall patient survival is poor.

Key words: malnutrition, cancer, albumin, handgrip strength, phase angle

Introduction

Cancer is a global health challenge with growing incidence, morbidity, and mortality (1). Malnutrition occurs frequently in oncology patients due to effects of the disease and of disease therapies on patients' nutritional status (2). It is associated with adverse outcomes and decreased survival (3, 4) and impairs quality of life (QoL) (5, 6). Supportive nutritional therapy has been beneficial for outcomes and QoL of cancer patients (7-9). Thus, determining nutritional status in oncology patients is essential. Several tools have been described to pursue this objective. One of these is the bioelectrical impedance analysis (BIA) that is used for the determination of body composition and has previously been used for oncology patients (10, 11). A reliable parameter obtained during BIA measurements is the phase angle (PA), which is derived from changes in resistance and reactance as an alternating current passes through tissues causing a phase shift (12). PA is one of the most widely accepted parameters for nutritional status in cancer and other patients (13-15). Another more recently developed tool is handgrip strength (HGS) obtained by measuring static muscle strength with handgrip dynamometers. It was originally used for functional examination in hand surgery but has re-

cently been proposed for the evaluation of nutritional status by several authors (16-18). Low HGS is associated with malnutrition and cachexia (19, 20). HGS has also been evaluated as a prognostic tool in surgical and cancer patients and is applied in epidemiological studies (21, 22). Furthermore, some biochemical markers are used as parameters for nutritional status. Serum albumin levels have been used to evaluate the nutritional state of oncology patients, but also of non-oncology patients in some studies (23, 24). In clinical practice, it is still used for this purpose. Moreover, albumin is a prognostic marker for clinical outcomes, e.g. it predicts the risk for anastomotic leakage in colorectal surgery (25, 26). In addition to physiological and biochemical measurement methods, scoring systems have been developed to screen for nutritional risk. The nutritional risk screening (NRS 2002) was introduced to identify patients who are likely to benefit from nutritional support (27). It has been suggested to indicate malnutrition in head and neck cancer patients (28) and was found to help predict postoperative complications and prolonged hospital stay in gastric cancer (29).

Even though all these different tools are available, it still remains unclear which method is the best choice for which group of patients. In view of the increasing worldwide importance of oncology patients, for whom particular attention to nutritional status is of utmost importance – especially at advanced disease states – the objective of the present study was to compare the above-mentioned tools to assess the nutritional status of these patients. Therefore, the primary aim of this study was to evaluate HGS, PA, albumin, NRS and QoL as markers for nutritional status in cancer patients with parenteral nutritional therapy. Moreover, parameters were assessed for possible prognostic qualities as pertains to patient survival.

Patients and Methods

Ethics Approval

Ethics board approval was obtained from the Medical Ethics Commission II of the Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany (No. 2013-573N-MA). The study was performed according to the Declaration of Helsinki.

Patients

Eligible for this study were oncology patients with malnutrition and parenteral nutritional therapy treated at the Outpatient Nutrition Clinic at the University Hospital Mannheim between August 2013 and November 2015. The Outpatient Nutrition Clinic at our institution treats 60 oncological patients with parenteral nutritional support per year. All consecutive patients for whom there was no exclusion criterion and who were willing to consent to study participation were included. The inclusion of patients was complicated by the fact that oncological patients with parenteral nutrition therapy often present in advanced tumour stages. Exclusion criteria were: patients under 18 years of age, the presence of an implanted cardiac pacemaker and/or defibrillator and/or obvious impairments of measurement methods. Indication for parenteral nutrition had to be confirmed by the treating physicians and followed the criteria of the European Working Group on Sarcopenia in Older People (30). Patients of both sexes were included. Informed consent was obtained from all patients.

Technical measurements (BIA and HGS), NRS and QoL assessment were carried out on the same day. Blood samples for the determination of serum albumin were taken within 7 days before or after the day of the other measurements.

Patient survival was determined from review of medical records or from information obtained from the patients' treating physicians or family doctors.

Bioelectrical Impedance Analysis

After a period of physical rest for at least 30 minutes, BIA measurements were performed by applying four gel electrodes, with two detecting electrodes placed at the ulnar aspect of the wrist and the medial malleolus of the dominant body side, following standard protocols. Electrodes were connected to a multiple frequency BIA instrument (*Nutriguard-M*, Data Input GmbH, Frankfurt, Germany). Measurements were digitally recorded and calculations for body composition values were performed using the *Nutriguard Plus* Software Version 5.4. As cut-off values for PA indicating malnutrition, individual age and sex specific threshold values were used as provided by the manufacturer (Data Input GmbH, Frankfurt, Germany).

Static Muscle Strength

A Saehan *Hydraulic Hand Dynamometer SH5001* (Saehan Corporation, Changwon, South Korea) was used to determine HGS. Measurements were conducted first on the dominant, then on the non-dominant hand. For this investigation, patients sat in a comfortable position with a 90° angle at the elbow joint. Patients were asked to squeeze the dynamometer using their maximum strength. Measurement was repeated after a break of 30 seconds. In total, three measurements for each hand were recorded. The mean value of the three efforts was calculated and used for this study. This procedure is similar to previous investigations (31, 32).

Serum Albumin Levels

Serum albumin levels were determined via standard laboratory procedures from venous blood samples acquired from patients after inclusion in this study. Hypalbuminaemia indicating malnutrition was defined as a serum albumin level < 30 g/L.

Nutritional Risk Screening (NRS 2002)

Nutritional screening was performed using the Nutritional Risk Screening (NRS 2002) (27) following guidelines of the European Society of Parenteral and Enteral Nutrition (ESPEN) (33). Patients were regarded as nutritionally at-risk when an individual score ≥3 was observed.

Short Form 12 (SF-12) Questionnaire

Physical Health Composite Score (PCS) and Mental Health Composite Score (MCS) obtained from the Short Form Health Survey (SF-12) were used to assess QoL.

Statistical Analysis

Quantitative approximately normally-distributed parameters are presented by mean values and standard deviations; for skewed data, median and range are given. Qualitative data is described by its absolute and relative frequency. For approximately normally-distributed data, two sample t-tests have been used in order to compare the mean values of two groups. For skewed variables, Mann–Whitney U-tests were performed instead. For the comparison of qualitative parameters Fisher's exact tests were applied. Correlation values for interval and ratio variables were determined by calculating Pearson's correlation coefficient, and, for ordinal variables, a Spearman correlation coefficient was calculated. A logistic regression model was used to identify factors associated with an elevated risk of postoperative complications, expressed as the odds ratio (OR) (95% confidence interval (CI)). Furthermore, regression was used as a multiple statistical method to identify risk factors. For this technique, several factors were included in the model; the most important factors were selected by stepwise elimination. Survival curves were generated using the Kaplan–Meier method. All statistical tests were two-tailed, and the threshold for statistical significance was set to $P < 0.05$. All analyses were performed using the SAS software, release 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

Between August 2013 and November 2015, 36 oncology patients were included in the study, 16 males (44.4%) and 20 females (55.6%). The mean age was 62.6 years. All included patients received parenteral nutrition for the treatment of malnutrition. The most frequent oncologic diagnosis was cancer of the gastrointestinal tract (GIT) (47.2%), including the upper-GIT *n*=13 (36.1%) and lower-GIT *n*=4 (11.1%). Other entities included cancer of the lung (16.7%), breast (8.3%), and prostate gland (5.6%) (Table 1).

Table 1. Patients' characteristics

Sex (n)	Male	16	(44.4%)
	Female	20	(55.6%)
Age (mean)		62.6	(30-87)
Type of primary cancer (n)			
	Gastrointestinal	17	(47.2%)
	Lung	6	(16.7%)
	Breast	3	(8.3%)
	Prostate	2	(5.6%)
	Other	8	(22.2%)
BMI (mean, kg/m2)		20.9	(15.6-32.0)
Albumin (serum, g/L)		24.8	(15.6-34.6)

Body Mass Index and Serum Albumin Levels

The mean BMI was 20.9 kg/m^2 (SD 4.2 kg/m^2; range 15.6-32.0 kg/m^2). The mean serum albumin level (*n*=30) was 24.8 g/L (SD 5.2 g/L; range 15.6-34.6 g/L) (Table 1). None of the patients in our study showed albumin levels within the reference range, all patients presented with hypoalbuminemia.

Handgrip Strength of the Dominant Hand

The mean value of the dominant hand was 21.6 kg for all patients (SD 8.9 kg; range 11.0-51.7 kg). The mean value for females was 16.2 kg (SD 4.5 kg; range 11.0-26.0 kg), the mean value for males was 28.1 kg (SD 8.9 kg; range 13.3-51.7 kg) (Table 2). These values were lower than the expected values of healthy individuals matched for sex and age.

Bioelectrical Impedance Analysis

The phase angle reflects the quality of the lean body mass. An average of 3.9° was observed. The mean lean body mass itself was 47.2 kg. These data and values for body cell mass, extracellular mass, body fat and body water are presented in Table 2.

NRS Score and Short Form 12

Both the median and the mode score in the Nutritional Risk Score was 5 points (Figure 1). The maximum score of 7 points was achieved by one patient, and the lowest score recorded was 2 points, which was observed in 3 patients. In the SF-12 questionnaire, the mean score of PCS was 29.5 points (SD 9.0; range 13.4-49.8) and the mean score of MCS was 36.1 points (SD 11.0; range 14.2-63.9).

Table 2. Results of handgrip measurement and bioelectrical impedance analysis

	unit	mean	SD
Handgrip strength dominant hand	kg	21.6	8.9
Phase angle	degree	3.9	0.9
Lean body mass	kg	47.2	11.5
Body cell mass	kg	18.9	4.8
Body cell mass of lean body mass	%	38.5	6.5
Extracellular mass	kg	29.2	8.4
Body fat	kg	10.8	10.4
Body fat	%	16.7	13.3
Body water	L	34.6	8.5

Handgrip Strength as a Reliable Marker for Nutritional Status

In univariate analysis, body cell mass (r=0.61, p < 0.0001), body water (r=0.41, p = 0,0141), PA (r=0.39, p=0,0182), lean body mass (r=0.36, p=0.0334), and the ratio of body cell mass on lean body mass (r=0.34, p=0,0398) showed significant correlation with handgrip strength. However, when the influence of gender (female versus male) was considered (p<0.0001) and multiple regression analysis was performed, only the factors gender (p<0,0001), PA (p=0.0168), and ratio of body cell mass on lean body mass (p=0.0172) were independent factors with significant influence on HGS (Table 3). No statistically significant impact on HGS was discovered for serum albumin levels (r=0.01, p=0.9492), BMI (r=-0.04, p=0.8183) or patient age (r=-0.27, p=0.1166).

Serum Albumin Levels Compared to Screening Parameters for Nutritional Status

Univariate analysis showed no significant correlation of serum albumin levels with the other parameters (*n*=30). When analysis of contingency tables was

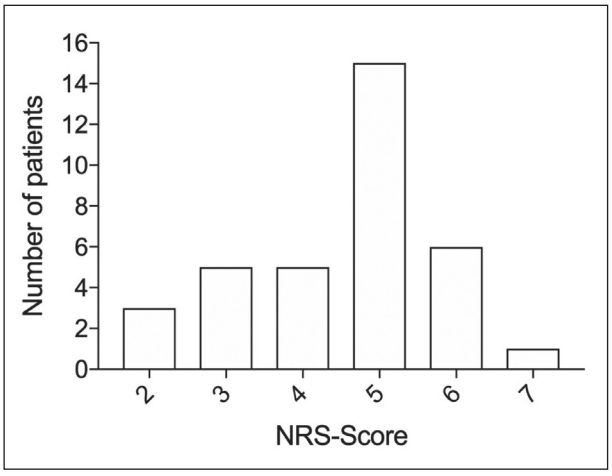

Figure 1. Distribution of NRS-Scores

Table 3. Independent factors influencing handgrip strength (dominant hand)

	p-value
Sex	< 0,0001
Phase angle	0,0168
BCM/LBM	0,0172

performed for albumin and PA (PA set as the gold standard measurement for body composition), a sensitivity of 83% (serum albumin levels < 30 g/L) and a specificity of 33% (serum albumin levels great than or equal to 30 g/L) was calculated in comparison to PA. Reference ranges for PA in this analysis were matched for age and gender; no values above the reference range were observed.

Nutritional Risk Score Compared to Screening Parameters for Nutritional Status

Statistical analysis revealed a negative correlation of NRS-scores with BMI (r=-0.46, p=0,0062), body fat (kg) (r=-0.45, p=0.0071), and body fat percent (r=-0.35, p=0.0405). This is not surprising since BMI is included in NRS screening. However, contingency table analysis of NRS regarding PA as the gold standard measurement for body composition showed a high sensitivity of 93% (NRS scores >=3) but a low specificity of only 17% (NRS scores < 3) for NRS predicting PA. Reference ranges for PA in this analysis were matched for age and gender; no values above the reference range were observed.

Results of Short Form 12 Questionnaire in Nutritional Screening

Results of the SF-12 questionnaire showed a significant correlation of the PCS with serum albumin levels (r=0.42, p=0.0288). Beyond that, no further significant correlation was found for PCS or MCS with the other parameters. Quality of life assessment did not correlate with PA and HGS measurements and was not significantly related to overall patient survival.

Survival Analysis and One-Year Follow-up

Survival analysis was performed for patients who completed a 1-year follow-up, or, for deceased patients. One patient committed suicide and was therefore excluded from the analysis. Loss of follow-up occurred in 2 cases. In total, 33 of 36 patients in this study (92%) were included in the Kaplan-Meier analysis (Figure 2). Median survival was 62 days with a 1-year survival-rate of 15%. A rapid decrease in survival occurred in the early observation period.

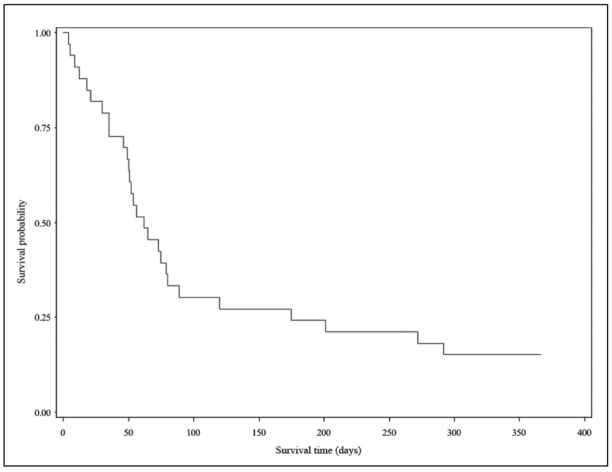

Figure 2. Kaplan-Meier analysis of survival

Discussion

In this prospective clinical study, we examined several surrogate parameters for malnutrition in a group of 36 cancer patients who received parenteral nutritional therapy for malnutrition between August 2013 and November 2015. Furthermore, patient survival was evaluated.

Main finding was that HGS is, compared to other parameters such as BMI and serum albumin, a reliable parameter for nutritional status in oncology patients with malnutrition. Moreover, the 1-year survival rate of only 15% indicates that confirmed indication for parenteral nutritional support in oncology patients comes along with poor overall survival.

HGS has been reported to predict survival in advanced cancer patients in some studies (34), but other studies failed to reproduce these findings (11). For BIA measurements and PA, which was regarded as the gold standard for body composition in our study, prognostic value in different clinical settings, including oncology and surgery, has been described (35, 36). Both PA and HGS can be used to predict post-interventional body composition in bariatric patients (32). HGS is lower in patients with malnutrition and colorectal cancer before tumor resection (10).

In our study, we found a significant correlation of HGS with PA, indicating that HGS may be a reliable parameter for the assessment of nutritional status in oncology patients. This is particularly relevant, since HGS measurement is suitable for clinical practice,

compared to alternative methods, because HGS is very simple to obtain, non-invasive, and inexpensive.

In clinical practice, albumin is used to determine patient nutritional status, e.g. when parenteral nutrition is applied in the course of "preoperative patient optimization" prior to surgical procedures low serum albumin levels are measured. However, albumin is not a sole nutritional marker because it is influenced by various conditions such as impaired liver function, volume status and inflammatory states including cancer (37). It is a negative acute phase protein (38), and oral protein intake does not influence serum albumin levels in some studies (39). Nevertheless, ESPEN guidelines for enteral nutrition consider albumin levels for the identification of patients nutritionally at risk. Our data do not indicate that albumin is a reliable marker for malnutrition. However, it can be used complementary since it is non-invasive, easy to obtain and cost-effective. All individuals in our study showed hypoalbuminemia, a fact that likely explains why our data did not demonstrate a significant prognostic effect of albumin levels on overall survival, as was demonstrated by other authors (40).

The NRS 2002 system was introduced to identify patients who are likely to benefit from nutritional support (22) and was shown to be a reliable tool in this regard (23). In our study, we found high sensitivity, but poor specificity of NRS, predicting PA. A possible explanation for this is the small number of patients with NRS scores < 3, and PA values within the reference range which limits statistical power. Some authors found data indicating that the NRS system was able to predict more postoperative complications and longer hospital stays in oncology patients (24). Contrary to this, in other studies, NRS scores >= 3 were associated with postoperative complications but did not turn out to be independent predictors when multivariable analysis was performed (38). Other data suggest that nutritional support based upon NRS 2002 screening might even result in over-nutrition (23). Our study failed to demonstrate prognostic significance of NRS as relates to survival. Since specificity compared to PA was low, other parameters might turn out to be more reliable for nutritional screening.

Patients in our study showed poor overall survival with a median survival of 62 days. The limited survival was not surprising since oncology patients with confirmed indication for parenteral nutrition are likely to be in poor general condition, have significant comorbidities, and present in advanced tumour stages. In other studies, survival ranges from 4 to 9 months for advanced pancreatic cancer (41) and is about 12 months for metastatic gastric cancer (42) and adenocarcinoma of the oesophagus (43). Moreover, this explains the small number of patients in our study, because patients with end-stage oncological diseases are generally hard to include in clinical trials.

Our data shows that oncology patients who require parenteral nutritional support are exposed to considerable health risks including reduced survival. Further investigation is needed to determine whether this can be improved by earlier nutritional screening and intervention. In this context, HGS and PA measurements seem to be the most useful, reliable, and easy-to-implement tools.

The validity of our study is limited due to the small number of patients and the heterogeneity of the study population. For these reasons, detailed statistical analysis of tumour stages and their entities could not be performed.

Conclusions

HGS is a reliable tool for the assessment of nutritional status in oncology patients. In this respect, BMI, NRS and QoL assessment seem to be less useful. Serum albumin is a prognostic tool in various clinical conditions, but alone, it is not particularly suitable for the diagnosis of malnutrition. The prognosis of oncology patients with indication for parenteral nutritional therapy is poor, which is reflected in low survival rates.

Conflict of interest

All authors have read and understood the policy on declaration of interests. The research reported in this study was supported by *B. Braun Melsungen AG*, Melsungen, Germany, which develops products related to the research being reported. The terms of this arrangement have been reviewed and approved by the Department of Surgery, University Hospital Mannheim, Faculty of the University of Heidelberg, in accordance with its policy on objectivity in research. The authors of this study have no further professional affiliation with *B. Braun Melsungen AG*.

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